

WHAT IS CLAIMED IS:

1. An isolated nucleic acid molecule comprising a sequence of nucleotides that encodes a rhesus monkey dickkopf-1 (rhDkk-1) protein as set forth in SEQ ID NO:2.
2. An isolated nucleic acid molecule comprising a sequence that encodes a polypeptide comprising the sequence set forth in SEQ ID NO:2 with 1- 10 amino acid additions, deletions, or substitutions, wherein the polypeptide binds low-density lipoprotein receptor related protein 5 (LRP5).
3. The isolated nucleic acid molecule of claim 1 wherein the nucleic acid is DNA.
4. The isolated nucleic acid molecule of claim 1 wherein the nucleic acid is mRNA.
5. The isolated nucleic acid molecule of claim 1 wherein the nucleic acid is cDNA.
6. The isolated nucleic acid molecule of claim 1 wherein the sequence of nucleotides comprises the sequence of nucleotides set forth in SEQ ID NO:1.
7. A vector comprising the nucleic acid molecule of claim 1.
8. A host cell comprising the vector of claim 7.
9. A process for expressing a rhesus monkey dickkopf-1 (rhDkk-1) protein in a recombinant host cell, comprising:
 - (a) introducing a vector comprising the nucleic acid of claim 1 into a suitable host cell; and,
 - (b) culturing the host cell under conditions which allow expression of said rhesus Dkk-1 protein.

10. An isolated and purified rhesus dickkopf-1 (rhDkk-1) polypeptide comprising a sequence of amino acids as set forth in SEQ ID NO:2.

11. An antibody that binds specifically to the polypeptide of claim 10

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12. A method for determining whether an analyte is an antagonist of Dickkopf 1 (Dkk-1) comprising:

- (a) providing a polypeptide comprising the extracellular domain of a Dkk-1 receptor;
- 10 (b) contacting the polypeptide with a rhesus monkey Dkk-1 (rhDkk-1) and the analyte; and
- (c) determining whether binding of the rhDkk-1 to the polypeptide is decreased in the presence of the analyte, wherein a decrease in the binding indicates that the analyte is an rhDkk-1 antagonist.

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13. The method of claim 12, wherein the Dkk-1 receptor is low-density lipoprotein receptor related protein 5 (LRP5) or low density lipoprotein receptor related protein 6 (LRP6).

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14. The method of claim 12, wherein the Dkk-1 receptor is kremen1 or kremen2.

15. The method of Claim 12 wherein the rhDkk-1 is labeled.

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16. The method of Claim 12 wherein the rhDkk-1 is a fusion protein.

17. A method for determining whether an analyte is an antagonist of Dickkopf-1 (Dkk-1) protein, which comprises:

- (a) providing a recombinant cell which produces one or more
- 30 Dkk-1 receptors;
- (b) introducing a reporter expression vector into the recombinant cell which comprises a reporter gene operably linked to a promoter responsive to Wnt-mediated signal transduction to provide a second recombinant cell;
- (c) exposing the second recombinant cell to the analyte and to a
- 35 rhesus monkey Dkk-1 (rhDkk-1); and

(d) measuring expression of the reporter gene, wherein an increase in expression of the reporter gene in the presence of the analyte relative to expression of the reporter gene in the absence of the analyte indicates that the analyte is a Dkk-1 antagonist.

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18. The method of Claim 17 wherein the one or more Dkk-1 receptors are selected from the group consisting of low-density lipoprotein receptor protein 5 (LRP5), low-density lipoprotein receptor protein 6 (LRP6), kremen1, kremen2, and combinations thereof.

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19. The method of Claim 17 wherein the promoter comprises one or more lymphoid enhancer factor/T cell factor (TCF/LEF) binding sites.

20. The method of Claim 17 wherein the rhDkk-1 is provided exogenously as an isolated rhDkk-1 protein or as a component of a medium obtained from a culture comprising a second recombinant cell which expresses the rhDkk-1.

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21. The method of Claim 17 wherein the rhDkk-1 is provided by cotransfecting the second recombinant cell with an expression vector encoding the rhDkk-1.

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22. The method of Claim 17 wherein a Wnt ligand is provided exogenously to the second recombinant cell in step (c) as an isolated Wnt ligand or as a component of a medium obtained from a culture comprising a second recombinant cell which expresses the Wnt ligand.

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23. The method of Claim 17 wherein a Wnt ligand is provided to the second recombinant cell by cotransfecting the second recombinant cell with an expression vector encoding the Wnt ligand.

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24. A method for determining whether an analyte interferes with binding of Dickkopf-1 (Dkk-1) protein to a Dkk-1 receptor, which comprises:

(a) providing a recombinant cell which expresses the Dkk-1 receptor;

(b) culturing the recombinant cell in a culture medium which contains a rhesus monkey Dkk-1 (rhDkk-1) protein and the analyte; and

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(c) measuring the rhDkk-1 bound to the rhDkk-1 receptor, wherein a decrease in the rhDkk-1 protein bound to the Dkk-1 receptor in the presence of the analyte relative to rhDkk-1 protein bound in the absence of the analyte indicates that the analyte interferes with the binding of the Dkk-1 protein to the Dkk-1 receptor.

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25. The method of Claim 24 wherein the Dkk-1 receptor is selected from the group consisting of low-density lipoprotein receptor protein 5 (LRP5), low-density lipoprotein receptor protein 6 (LRP6), kremen1, kremen2, and combinations thereof.

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26. The method of Claim 24 wherein the rhDkk-1 is labeled.

27. The method of Claim 24 wherein the rhDkk-1 is a fusion protein.

28. A method of identifying an analyte that induces Wnt signaling comprising:

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(a) transfecting a recombinant cell expressing one or more Dkk-1 receptors with a reporter gene operably linked to a promoter responsive to Wnt-mediated signal transduction;

(b) exposing the cells to an analyte, rhesus monkey Dkk-1 (rhDkk-1), and a Wnt ligand;

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(c) measuring expression of the reporter gene, wherein an increase in expression of the reporter gene in the presence of the analyte relative to expression of the reporter gene in the absence of the analyte indicates that the analyte induces the Wnt signaling.

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29. The method of Claim 28 wherein the one or more Dkk-1 receptors are selected from the group consisting of low-density lipoprotein receptor protein 5 (LRP5), low-density lipoprotein receptor protein 6 (LRP6), kremen1, kremen2, and combinations thereof.

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30. The method of Claim 28 wherein the promoter comprises one or more lymphoid enhancer factor/T cell factor (TCF/LEF) binding sites.

31. The method of Claim 28 wherein the rhDkk-1 is provided exogenously as an isolated rhDkk-1 protein or as a component of a medium obtained from a culture comprising a second recombinant cell which expresses the rhDkk-1.

5 32. The method of Claim 28 wherein the rhDkk-1 is provided by cotransfecting the recombinant cell with an expression vector encoding the rhDkk-1.

33. The method of Claim 28 wherein the Wnt ligand is provided exogenously as an isolated Wnt ligand or as a component of a medium obtained from a
10 culture comprising a second recombinant cell which expresses the Wnt ligand.

34. The method of Claim 28 wherein the Wnt ligand is provided by cotransfecting the recombinant cell with an expression vector encoding the Wnt ligand.

15 35. A method for determining whether a compound inhibits Dickkopf 1 (Dkk-1) protein suppression of osteoblast differentiation comprising:

(a) providing pluripotent cells which can be induced to differentiate along an osteoblast lineage;

(b) transfecting the cells with a first expression vector which
20 expresses a rhesus monkey Dkk-1 (rhDkk-1) protein, a second expression vector, which expresses low-density lipoprotein receptor protein (LRP), and a third expression vector which expresses Wnt protein;

(c) incubating the cells in a medium containing the analyte for a time sufficient for expression of the rhDkk-1 protein, LRP, and Wnt protein; and

25 (d) measuring expression of one or more osteoblastic markers wherein expression of the one or more markers indicates that the analyte inhibits rhDkk-1 suppression of osteoblast differentiation.

36. The method of Claim 35 wherein the pluripotent cells are pluripotent
30 marrow stromal cells or pluripotent mesenchymal cells.

37. The method of Claim 35 wherein the pluripotent cells are selected from the group consisting of ST2 cells and C3H10T1/2 cells.

38. The method of Claim 35 wherein the one or more osteoblastic markers are selected from the group consisting of alkaline phosphatase, Bglap, and Runx2.